a central component of the mechanism, he called it the *chemiosmotic* hypothesis.

Mitchell's proposals were initially extremely controversial, giving rise to what are often referred to as the *ox phos wars* (Prebble, 2002). The opposition was partly empirical – for example, questioning the evidence for the claimed proton gradient – and partly theoretical. The idea of a proton gradient across a membrane was foreign to most biochemists, who were still oriented to the soluble systems model for explaining metabolic processes. Remarks of Efraim Racker reveal the combative nature of the debate: He referred to "hypothetical proton gradient and imaginary membrane potential" and compared Mitchell's claims to "pronouncements of a court jester or a prophet of doom" (Racker, 1975). Yet, at approximately the same time Racker wrote to the central figures investigating oxidative phosphorylation – Paul Boyer, Britton Chance, Lars Ernster, Tsoo E. King, Henry A. Lardy, and D. Rao Sanadi, in addition to Green, Lehninger, Mitchell, and Slater – proposing the preparation of a joint statement designed to reduce the acrimony over oxidative phosphorylation. Although negotiations over the joint review were tempestuous, several of the authors agreed on a joint introductory statement, followed by individual papers, that appeared in the *Annual Review of Biochemistry* for 1977 (Boyer et al., 1977).[25] By this time Racker had been convinced of the chemiosmotic hypothesis and his own contribution supported Mitchell's position. Although controversy continued, Mitchell was awarded the Nobel Prize in 1978, a testimony to the significance of his proposal in transforming thinking about the phosphorylation process.

With the incorporation of Mitchell's account of the linkage between electron transport and phosphorylation, the mechanism of oxidative phosphorylation was essentially resolved. Moreover, the account wove together in a fundamental way morphological structure with chemical operations. Palade's cristae not only were seen to contain the critical enzymes of electron transport in a spatially organized manner (the functional significance first attached to them), but also served to create the proton motive force that drove ATP synthesis. The stalks and spherical particles attached to the membrane housed F_0 and the ATPase and could respond to the proton gradient by synthesizing ATP. The combined contributions of studies of cell structure and biochemical function were melded into a comprehensive account of the mechanism that accounted for the phenomenon. Many details of the operation of the

[25] Racker (Interview, 1989, Ithaca, NY) expressed dissatisfaction with the final result since each author ended up arguing for his own position rather than engaging the others in the manner he had hoped.